MEDICAL PROCEEDINGS

MEDIESE BYDRAES

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EDITORIAL · REDAKSIONEEL

POISONS, POTENTIALLY HARMFUL AND HABIT-FORMING DRUGS

OBLIGATIONS OF MEDICAL PRACTITIONERS UNDER THE MEDICAL, DENTAL AND PHARMACY ACT, NO. 13 OF 1928

The Union Health Department has from time to time drawn attention to certain requirements of this Act with which medical practitioners must comply.

As our colleagues lay themselves open to certain penalties if they fail to conform with the requirements of the Act, we strongly endorse the request of the Union Health Department that they co-operate fully in observing the legal requirements.

The Act *inter alia* requires the following:

1. That every medical practitioner who dispenses a medicine containing a poison listed in the 4th Schedule or a potentially harmful drug listed in the 6th Schedule to the Medical, Dental and Pharmacy Act, shall maintain records in a *Day Prescription Book* wherein appear the following:

(*a*) The date of supply of the drug dispensed.
(*b*) The name and address of the patient to whom the drug was supplied.
(*c*) The name and quantity of the drug supplied.

2. That in addition to the keeping of the *Day Prescription Book,* it is incumbent on every medical practitioner who supplies or dispenses a *habit-forming drug* to keep a register known as a *Habit-Forming Drug Register* in which the following data must be recorded:

Receipt Side:

(*a*) Supplier's name and address.
(*b*) Date on which the supply of drugs was received.

GIFSTOWWE, MOONTLIKE NADELIGE EN GEWOONTEVORMENDE MIDDELS

VERPLIGTINGE VAN MEDIESE PRAKTISYNS KRAGTENS DIE WET OP GENEESHERE, TANDARTSE EN APTEKERS, NO. 13 VAN 1928

Die Unie-departement van Gesondheid het van tyd tot tyd die aandag gevestig op sekere vereistes van hierdie Wet waaraan mediese praktisyns moet voldoen, vir sover dit gifstowwe en gewoontevormende middels betref.

Aangesien ons kollegas hulself aan sekere strawwe blootstel as hulle versuim om aan die bepalings van die Wet te voldoen, vereenselwig ons ons geheel en al met die versoek van die Unie-departement van Gesondheid, nl. dat hulle volkome moet saamwerk om die regsvereistes na te kom.

Die Wet vereis onder meer die volgende:

1. Dat iedere mediese praktisyn wat medisyne opmaak, bevattende 'n gif genoem in die 4de Bylae, of 'n moontlike nadelige middel genoem in die 6de Bylae van die Wet op Geneeshere, Tandartse en Aptekers, aantekening daarvan moet maak in 'n *Dag-preskipsieboek* waarin die volgende besonderhede verstrek moet word:

(*a*) Die datum waarop die voorbereide medisyne verskaf is.
(*b*) Die naam en adres van die pasiënt aan wie die middel verskaf is.
(*c*) Die naam en hoeveelheid van die middel wat gebruik is.

2. Dat, benewens die byhou van die *Dagpreskripsie boek,* dit die plig is van iedere mediese praktisyn wat 'n *gewoontevormende middel* verskaf of berei om 'n register, bekend as die *Register van Gewoontevormende*

(*c*) Quantity of drugs received.

Issue Side:

(*a*) Date of issue of the drug.

(*b*) Name and address of the patient who receives the drug.

(*c*) Quantity of the drug supplied.

All *Habit-Forming Drug Registers* (not the *Day Prescription Book*) must be balanced on the last day of March, June, September and December of each year, so as to show the actual quantity of the drug remaining in stock on these dates.

3. That every individual medical practitioner must use all reasonable care in the use and storage of poisons and habit-forming drugs. (*Vide* Sections 54 and 61 (4)).

4. That every individual medical practitioner who dispenses a medicine shall label the container with his name and professional address. (Section 56).

5. That it is the legal obligation of every medical practitioner to familiarize himself with the requirements of the Act and the contents of the Schedules.

Medical practitioners are also asked to note that:

Copies of the *Habit-Forming Drug Register* may be obtained from the Registrar of the South African Pharmacy Board, Pretoria; alternatively, a record may be maintained in a *bound book* specially kept for this purpose, wherein are recorded the data under the relevant headings.

The lists of drugs classified in Schedule 4 (Poisons) and Schedule 6 (Potentially Harmful Drugs) of the Act were published in Government Proclamations numbered 209 and 216 of 1957.

A list of habit-forming drugs classified under the 5th Schedule of the Act will be published in a forthcoming issue of *Medical Proceedings*.

Middels, daarop na te hou waarin die volgende gegewens aangeteken moet word:

Ontvangskant:

(*a*) Leweransier se naam en adres.

(*b*) Datum waarop 'n voorraad van die middel ontvang is.

(*c*) Die hoeveelheid wat ontvang is.

Uitreikingskant:

(*a*) Datum waarop die middel uitgreik is.

(*b*) Naam en adres van die pasiënt wat die middel ontvang het.

(*c*) Hoeveel van die middel verskaf is.

Alle *Registers van Gewoontevormende Middels* (nie die *Dag-preskripsieboek* nie) moet afgesluit word op die 1ste dag van Maart, Junie, September en Desember van iedere jaar, om die werklike hoeveelheid van hierdie middels in voorraad op die genoemde datums, aan te toon.

3. Dat iedere individuele mediese praktisyn alle redelike sorg aan die dag moet lê vir sover dit die gebruik en die wegbêre van gifstowwe en gewoontevormende middels betref. (Lees Artikels 54 en 61 (4)).

4. Dat iedere individuele mediese praktisyn wat 'n geneesmiddel berei, 'n etiket, aantonende sy naam en professionele adres, op die houer moet plak. (Artikel 56).

5. Dat daar 'n regsverpligting op iedere mediese praktisyn rus om homself vertroud te maak met die bepalings van die Wet en die inhoud van die Bylaes.

Mediese praktisyns word ook gevra om daarop te let dat:

Eksemplare van die *Register van Gewoontevormende Middels* verkrygbaar is by die Registrateur van die Suid-Afrikaanse Aptekersraad, Pretoria; so nie, kan aantekeninge gemaak word in 'n *gebinde boek* wat spesiaal vir hierdie doel gehou word, en waarin die gegewens, onder geskikte opskrifte, opgeteken moet word. (Bylae 1).

Die lys van middels wat in Bylae 4 (gifstowwe) en in Bylae 6 (moontlike nadelige medisyne (van die Wet geklassifiseer is, is in Staatsproklamasies nommer 209 en 216 van 1957 gepubliseer.

'n Lys van gewoontevormende middels, geklassifiseer in die 5de Bylae van die Wet, sal in 'n eersdaagse uitgawe van *Mediese Bydraes* gepubliseer word.

ABSTRACTS

PREDNISONE IN THE MANAGEMENT OF MYOCARDIAL INFARCTION

The authors used prednisone to treat patients with myocardial infarction who were suffering from shock or had at the same time high or prolonged fever, effusions into the pleura or pericardium or subacute pulmonary oedema with oliguria, persistent pain, or poor general condition. As a rule, 30 mg. prednisone was administered daily for the first 4–5 days. Once the E.S.R. reached sub-normal values, the doses were gradually reduced. The duration of therapy did not exceed 2–3 weeks.

The results were so favourable that the corticosteroids can be recommended as an additional measure in the treatment of myocardial infarction. Even where the patients had a high fever, the temperature could be brought down to afebrile levels within 24–48 hours. The E.S.R. did not return to normal for about 2 weeks. The subjective improvement, commented on spontaneously by almost all the patients, was impressive. Micturition was restored, and polyuria even set in in some cases. There is no danger of an effect on blood pressure or of a change in the electrolyte balance. If a symptomatic humeroscapular periarthritis or shoulder-hand syndrome develops following the infarction, the use of prednisone is by far the most effective treatment.

[Bouvrain, Y., Sikorav, H. and Abastado, M. (1959): Bull. Soc. Méd. Hôp. Paris, **75**, 539].

THE STEIN-LEVENTHAL SYNDROME

Eight typical cases of Stein-Leventhal syndrome were closely studied at the Women's Clinic of the University of Helsinki. This disease has the following symptoms: oligomenorrhoea or amenorrhoea, sterility, bilaterally enlarged ovaries with small cysts, and frequently also male hair distribution. None of these symptoms is characteristic, but all of them taken together provide a well-defined picture. The disease is presumably of hormonal origin, but the aetiological mechanism is still obscure.

The usual hormone analyses were performed, as well as fractionation of the urinary 17-ketosteroids. Thereupon a stimulating effect was exerted with chorionic gonadotropin (1,500 units daily for 3 days), and later with Cibacthen as well (40 units intramuscularly); the hormone levels were then determined again. Some months after surgery—partial oophorectomy, removal of the presacral sympathetic nerves—hormone analyses were once again performed.

In view of the clinical and histological data, the authors come to the conclusion that the Stein-Leventhal syndrome can be divided into two main types: the type with and the type without ovarian function. In the first type, the masculinising factor has its origin in the ovaries, presumably in the stroma. In the second type, pituitary gonadotropin, owing to the absence of ovarian function, probably acts on the 'sexual zone' of the adrenal cortex, which is the source of the masculinising factor in these cases.

[Pesonen, S., Timonen, S. and Mikkonen, R. (1959): Acta Endocr. (Den.), **30**, 405].

PERLON AND NYLON

Perlon and *nylon* are conspicuous for their low degree of *inflammability*. If a fabric made from such fibres comes into contact with a flame, it melts locally, but does not continue burning of its own accord. Thus, there is no need to fear that large areas of skin will be burnt if nylon or Perlon garments catch fire. Nor do these fabrics form toxic products of combustion which could exert a potentially poisonous effect as a result of inhalation or absorption through the skin.

[Ehrlicher, H. (1959): Medizinische (G.) 174].

PROTEIN DEFICIENCY IN SURGICAL PATIENTS

It has been demonstrated with increasing frequency in the course of recent years that deficient nutrition, especially an inadequate supply of protein, can significantly diminish the success of a surgical operation. Insufficient nutrition, leading to hypoproteinaemia and impaired liver function, increases the dangers of a surgical intervention as well as the possibilities of shock and infection. Intestinal oedema and hypotonia may develop, and healing of the wound may be delayed. Owing to the impairment in liver function, the risks attendant upon Pentothal or chloroform anaesthesia are increased in cases of deficient nutrition, with the result that post-operative liver failure is possible. That Pentothal is extraordinarily dangerous in the case of patients with nutritional deficiencies was brought home to the author by his own experience; animal experiments point in the same direction.

Prior to surgical interventions, therefore, measures should be taken to raise the serum protein levels as early as possible. For it appears that in cases of impaired liver function, for example, a 4-week diet rich in proteins is not sufficient to reduce the dangers of an operation. Hence, pre-operative prophylaxis also becomes a question of nutrition. The situation is of course particularly precarious in the case of emergency operations.

[Renes, G. J. (1959): Trop. Geograph. Med. (Netherlands), **11**, 44].

THE PATHOGENESIS OF NEPHROTIC SYNDROME

In nephrotic syndrome the permeability of the glomerular capillaries is increased with the result that proteins which are normally retained are excreted. The consequence of this albuminuria is a hypoproteinaemia associated with a fall in osmotic pressure and the formation of oedema. Albumin excretion alone, however, cannot fully account for the early appearance and the extent of the hypoproteinaemia. The suspicion that protein synthesis may be impaired has not been corroborated; it proved to be normal or even increased. The hypothesis that nephrotic syndrome is accompanied by hypothyroidism has also been proved false.

The oedema is more likely to be caused by the combined effect of the following factors: reduction in osmotic pressure; increase in anti-diuretic substances since the posterior pituitary is stimulated as a result of the diminution in the amount of circulating blood; increase in the sodium-retaining adrenocortical hormones, and hence secondary hyperaldosteronism. In addition, hypoproteinaemia seems to provoke a disorder in potassium metabolism, the potassium in the cells being excreted with the urine and replaced by sodium. The cause of hyperlipaemia is likewise still unaccounted for: a probable explanation is that the deposits of fat are mobilised as the result of the hypoproteinaemia and malnutrition.

[Quirno, N. (1958): Rev. Asoc. Méd. Argent., **72**, 213].

SEX CHROMATIN AND KLINEFELTER'S SYNDROME

Growing interest has recently been shown in Klinefelter's syndrome. Improvements in the field of cytological diagnosis have led to a better understanding of the embryological aspects of the disorder, and determination of the chromatin sex is now an accepted part of the endocrinological investigation.

Where the chromatin sex is found to be positive in a boy or a man, the diagnosis of Klinefelter's syndrome may be regarded as certain. In cases where the chromatin sex is negative, however, the diagnosis may still be justified if the patient has the clinical stigmata of the disease and if the histological picture obtained by testicular biopsy shows the irrefutable characteristics.

The authors describe the cases of two 14-year-old boys with Klinefelter's syndrome. In one of the boys, who had none of the clinical stigmata, the diagnosis was established by determination of the chromatin sex. In the other, who had gynaecomastia and hypogonadism, the chromatin sex was negative as in the normal male. Here, the diagnosis could be established only with the aid of testicular biopsy.

[Briggs, D. K., Epstein, J. and Kupperman, H. S. (1958): J. Urol., **80**, 57].

ADRENOCORTICAL HORMONES IN RATTLESNAKE BITES

Animal experiments were carried out in an attempt to confirm reports that corticosteroids have a beneficial therapeutic effect in cases of snake bite. It may be reckoned that the average bite of a rattlesnake releases enough venom to kill approximately 4 young pigs, or 12 dogs, or 46 rhesus monkeys. The acute toxicity of the crystalline venom (20–25% of the original weight) varies considerably for different species, the approximate lethal dose for dogs and rhesus monkeys being 0.64 mg. per kg., as compared for example with 3.2 mg. per kg. in pigs and guinea-pigs, and 25 mg. per kg. in rats.

Dogs were injected intramuscularly with rattlesnake venom in a dose high enough to kill all but 17% of the animals. In another experiment, dogs were given 100 mg. hydrocortisone intravenously either immediately after the injection of venom or 2 or 4 hours later; in addition, the animals were given 50 mg. hydrocortisone daily for a few more days.

Where hydrocortisone was injected immediately after the dose of venom, the survival rate was 100%. Where the injection was given after intervals of 2 and 4 hours, the survival rate dropped to 65 and 75% respectively. In their conclusion, the authors observe that the administration of hydrocortisone 'did not influence visibly the local proteolytic or septic effects or healing'. Thus, though the experiments confirmed the beneficial effect of the hormone, they failed to explain the reason for the good results obtained.

[Deichmann, W. B., Radomski, J. L., Farrell, J. J., MacDonald, W. E. and Keplinger, M. L. (1958): Amer. J. Med. Sci., **236**, 204].

[Kerr, M. M. (1959): Brit. Med. J., **1**, 902].

STORAGE OF LIVING CELLS

Living cells can be *stored* at −80°C. for many weeks. The freezing process is important. The best method is to place the material in Tyrode's solution with 15% glycerin and to cool it slowly at first down to −15°C., then more rapidly to −70°C. The cells are then stored in dry ice.

[Tran Ba Loc (1959): Rev. Franç. Études Clin. Biol., **4**, 76].

MEDICO-LEGAL SECTION

R. v. BUREKE*

THE DEFENCE OF PROVOCATION

(FEDERAL SUPREME COURT)

1959. *October* 14, 18. CLAYDEN, A.C.J., BRIGGS, F.J., and BEADLE, A.C.J. (S.R.).

Criminal law.—Murder.—Provocation.—"Defence" of.—Cannot succeed if subjectively the accused did not lose self-control.—Must have been done in heat of passion occasioned by sudden provocation.

On a charge of murder, in considering the 'defence' of provocation (which is only material if intent to kill has been established), although the objective test of a reasonable man's reaction to the provocation received must be applied in deciding whether loss of control was to be expected and also whether the acts done bore reasonable relation to the provocation, there remains also the subjective question whether the accused did lose his self-control.

The defence of provocation cannot succeed if subjectively the accused had not lost his self-control in the sense that his act was done in the heat of passion occasioned by sudden provocation. It is therefore the duty of the trial Court to consider the question whether the accused lost his self-control, not only in connection with the issue of intention to kill, but also in relation to the 'defence' of provocation.

Appeal from a conviction for murder in the High Court, Southern Rhodesia. The facts appear from the reasons for judgment.

O. J. Price, for the appellant, at the request of the Court.

C. J. Waddington, for the Crown.

Cur. adv. vult.

Postea (28 October).

BRIGGS, F.J.: The appellant was convicted by the High Court of Southern Rhodesia of the murder of his wife Ethel. The Court found that there were no extenuating circumstances and he was accordingly sentenced to death.

* Reprinted by permission of the publishers, Juta and Co., Ltd., from the *South African Law Reports,* 1960, (1), January.

The killing was never in dispute. The issues at the trial were, first, the appellant's intention, and secondly, provocation. The appellant inflicted about ten wounds with a knife, and death would have resulted from either of two of these wounds without other injury. The nature of the attack suggested *prima facie* an intent to kill. It was contended, however, that in consequence of provocation received by the appellant and loss of self-control resulting therefrom an intention to kill should not be inferred from his acts, and also that, even if an intention to kill was established, the provocation was sufficient to reduce the offence to culpable homicide.

Two days before her death the deceased had left her husband. There was some evidence that he had maltreated her to such an extent as might have justified her desertion, but this evidence was not such as would certainly have been accepted and there is no finding on it. The appellant suspected a liaison between his wife and one Robert and, though the Court found that their association was innocent, it cannot be said that the appellant's suspicions were wholly unreasonable. The appellant went to the kraal where his wife was working and told her that he had killed a chicken. By this he intended to ask that she should come home to cook it for him. She would not speak to him, but her silence made it clear, although he pressed his request, that she would not come. He then attacked her and she died the same night. In so far as the appellant's version of the facts differed from this I am clearly of opinion that the Court was right in rejecting it. The Court then said,

"The accused's anger arose from the fact that he invited his wife to return to him by his reference to the chicken he said he had killed, and her refusal annoyed him, and he then stabbed her. He may also have thought that his wife loved another for this is the reason that he gave his employer for his wife's departure. But even if we assume, in his favour, that he had some such belief and if we add to that his anger arising from his wife's refusal to return to him, this provocation did not deprive the accused of his self-control. For these reasons we are satisfied that the Crown has proved beyond reasonable doubt that the accused had the intent to kill. A proper verdict, therefore, is one of guilty of murder.'

I think the finding that the provocation did not in fact deprive the appellant of his self-control requires some examination. The only eye-witness of the attack was a small girl who appeared to be about seven or eight years old. Her evidence does not assist on this question. Having rejected the evidence of the appellant that Robert was present at the scene, the Court was left to decide the matter by inference from what had occurred before the attack, from the nature of the attack itself, and from the remainder of the appellant's statement to the police and statement in Court. On the preceding facts I think it would have been reasonable to infer that, when his efforts towards reconciliation failed, the wife's refusal to resume her conjugal duties would suddenly aggravate his suspicions of an adulterous relationship and might turn them into something like subjective certainty. The wounds indicated a wild and random attack. They did not suggest either a deliberate killing or a desire to punish by inflicting pain. On this material alone it would not have been unreasonable to infer that the appellant had lost control of himself. But that material did not stand alone. In his statement to the police the appellant described the attack and said, "I intended to kill her because he was in love with Native Robert." At the trial he did not seek to withdraw that admission and did not say or suggest that he had lost control of himself. He said, "I slapped her a blow with the open hand. She then sat down. I produced a knife and stabbed her." Read as a whole the two statements certainly suggest a deliberate, though not necessarily a premeditated, killing. I do not think this Court can interfere with the finding that the provocation did not deprive the accused of his self-control. And in view of that finding there can be no reason to interfere with the finding that the appellant intended to kill.

It was argued for the appellant that there was a misdirection, in that the Court considered the question of loss of self-control only in reference to formation of intention, and not in relation to provocation generally. It is, I think, implicit in the judgment of this Court in *R.* v. *Tenganyika**, 1958 R. & N. 228, that in considering the 'defence' of provocation (which is only material if intent to kill has been established), although the objective test of a reasonable man's reaction to the provoca-

* See 1958 (3) S.A. 7.—EDS.

tion received must be applied in deciding whether loss of control was to be expected and also whether the acts done bore reasonable relation to the provocation, there remains also the subjective question whether the accused did lose his self-control. I think this may be inferred from the Court's reference to sec. 141 of the Transkeian Penal Code, which requires that the act should have been done 'in the heat of passion occasioned by sudden provocation'. These words clearly refer to the sudden loss of emotional or mental balance which is commonly described as loss of self-control. I have no doubt whatever that this Court never intended to lay down that the defence of provocation could succeed if subjectively the accused had not lost his self-control in this sense. This point has been noticed by SCHREINER, J.A., in *R.* v. *Krull,* 1959 (3) S.A. 392 (A.D.) at p. 399, where he said,

'It is of course not contemplated that an accused who, though he was provoked, undoubtedly intended to kill should escape conviction of murder because ordinary people would have lost their self-control —though he did not.'

With this I respectfully agree; but I do not interpret *Tenganyika's* case as intending to lay down anything to the contrary.

I accordingly accept the submission that it was the duty of the trial Court to consider the question whether the appellant lost his self-control, not only in connection with the issue of intention, but also in relation to the 'defence' of provocation. I can see no sufficient reason for thinking that the Court did not do so. If it did, the defence must fail and there was no need to consider the objective tests. I think the finding of no loss of self-control was at large and governed this issue as it governed that of intent. But if I am wrong, I should still be of opinion that the defence of provocation inevitably failed, in that the attack went far beyond anything which a reasonable man of the appellant's community might have been expected to do in consequence of the provocation received. For these reasons I consider that the conviction of murder was correct and should be affirmed.

The Court gave reasons for its decision that there were no extenuating circumstances. They are as follows,

'It is contended on your behalf that the possibility that you may have thought that your wife loved another, together with your anger when she refused to return to you, has the effect of reducing the moral blame for the crime which you committed. We have considered this contention carefully and we are of the opinion that while these points explain your motive for killing your wife, they do not constitute extenuating circumstances. There will be a finding, therefore, that there are no extenuating circumstances in this case.'

It was submitted that, if the finding of no loss of self-control was erroneous, the case would fall within the principles laid down by this Court in *R.* v. *Tomasi,* 1956 R. & N. 2 at p. 4, in that the trial Court had 'excluded from its consideration a factor proper to be taken into account,' and the discretion had accordingly been exercised on an incorrect principle. It cannot, I think, be doubted that loss of self-control in consequence of provocation received may justify a finding of extenuating circumstances, though the defence of provocation is rejected, and, if this question had been improperly overlooked, this Court might have thought it proper to exercise its power to interfere with the finding. But on the finding of no loss of self-control, which must stand, it is impossible to say that the Court below has acted on a wrong principle, and this Court cannot interfere with a finding that there are no extenuating circumstances, unless the Court below has acted on a wrong principle or the decision is unreasonable on the facts. This decision certainly cannot be said to be unreasonable.

I think this Court should follow the practice of the Appellate Division in refraining from any expression of opinion whether extenuating circumstances 'might well, or apparently should, have been found by the trial Court.' See *R.* v. *Balla and Others,* 1955 (3) S.A. 274 (A.D.) at p. 275. As SCHREINER, J.A., there explains, having regard to the functions of the Executive after a death sentence, this practice is in the interest of unsuccessful appellants.

I would accordingly dismiss this appeal.

CLAYDEN, A.C.J., and BEADLE, A.C.J. (S.R.), concurred.

THE PHOTOCHEMISTRY AND PHOTOBIOLOGY OF THE SKIN*

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If one chooses to talk about the photobiology of the skin, starting from the light source and ending with the skin's response to it, one must cross many divisions of science. With the sun as our chief source of light, some parts of astronomy and meteorology are relevant. The action of light on the skin belongs partly to physical optics and photochemistry. Its effects will be governed by physiological and biochemical considerations and these, in turn, by genetic, immunological and pharmacological topics. The apparent end result is a subject for the clinician, physiologist or pathologist; and then, just as we seem to have finished, we may find that the light stimulus has wrought subtler delayed changes which alter the skin even for the distant future. In fact, as knowledge grows the uncertainties multiply prodigiously, and an innocent mechanistic approach helps us little. Biologists then are bound to look ridiculous when they try to bring a mechanically minded order into such a scheme. For good or ill, there are only a few topics in the photochemistry and photobiology of the skin which I shall discuss here. The errors and gaps are left to the attention of those better educated at the present time and in the future.

SUNLIGHT

Light reaching us from the sun traverses the earth's atmosphere, which acts as a window, letting through only certain ranges of wavelength. In the ultraviolet, visible and infrared range, light exhibits a property the reverse of one shown by X-ray and radium. For sunlight, the longer waves are more penetrating, while for X-rays the shorter rays penetrate farther. The shorter ultraviolet rays penetrate poorly and do not reach us. They are nonetheless able to split the bond of diatomic oxygen in the rarefied atmosphere, thus creating ionized layers which induce other chemical reactions and act as a reflecting layer for the longer radio waves. One result is the formation of ozone, which sinks well below the ionosphere to a level about 20–25 miles up. The ozone layer holds back the longer waves of the ultraviolet, virtually up to 3000 Å (1 Å $= 10^{-8}$ cm.), by means of which it is also re-converted to diatomic oxygen. So the shorter ultraviolet rays are of no direct interest to earth-bound creatures who do not intend to explore the solar system personally. Before leaving the subject of the more harmful ultraviolet rays, let me refer to the excellent study on Johannesburg sunlight made by Mr. S. J. Richards 20 years ago. He showed that the sunlight at Rietfontein was as intense in the 3000 Å regions as anywhere in the world, and certainly as rich at this end of the spectrum as at any supposedly health-giving Alpine resort.

EFFECTS OF LIGHT

When we discuss the action of light on matter the subject is signposted by the greatest names in the history of physics.

All substances absorb some parts of the light spectrum falling on them. The energy of light falling on an opaque piece of metal, for instance, is taken up by the metal's mobile electrons. When light is not absorbed, but becomes refracted, polarized, scattered or magnetically influenced during transmission, electromagnetic wave theories take charge of it. Chemical effects can, however, only be expected when light is absorbed. Although this principle has been expounded for over a hundred years, the quantitative aspects of the relations between light and matter were the notable contributions of Planck and Einstein in the early part of the 20th century. Light also heats, but the heating effect is less in the ultraviolet. Heating apart, the chemical effects of light are subject to some restrictions which I shall put into crude terms. Firstly, an all-or-none law holds: a photon (or light unit) is either used up totally in colliding with a particle of matter or else does nothing to it. Secondly, one cannot send a boy to do a man's job. Even a whole school full of boys won't do. This is to say that a photon has fixed energy and there is no summation at its absorption site. Thirdly, the man or boy on the job must have the 'know-how': a photon with a certain energy at its disposal

* A lecture delivered to a Scientific Staff Meeting at the S.A. Institute for Medical Research on 7 December 1959.

cannot necessarily be expected to do a particular job requiring that amount of energy.

When a non-ionizing photon (as in near ultraviolet or visible light) is absorbed by some part of a molecule, it may displace electrons from their normal orbitals without knocking them clear altogether. The molecule becomes more highly energized or 'excited', which is the first step in the changes due to light. It may then wobble so much as to tear apart an interatomic bond, depending on the bond energy involved. If the photon does not have an energy adequate to overcome the bond energy, this photolysis will not occur. Several standard equations exist which enable one to relate these energies to one another.

The excited molecule can give up its energy in various other ways, but a great deal depends on the freedom of movement of the molecules. Most situations in which the processes are better understood have been worked out on relatively simple gaseous reactions. The energy may be released in one stage or in a series of smaller jumps to progressively lower levels, like a cascade. Chains of energy transfer are thus brought about, at various points in which the energy may be 'trapped' for different periods. Some examples of this type of mechanism can be sought in the phenomena of electroluminescence and in photosynthesis. On the more recondite aspects, the recent Faraday Society discussions are of great interest.

How do these considerations apply to the skin? It would indeed be worth while knowing the answer. The most we can say is that even the well-studied processes are shrouded in mystery, and the obscure ones leave us guessing altogether. Whatever ultimately emerges, this is the physical framework which already exists to absorb the findings.

From this we may now turn to consider some specific examples from cutaneous photochemistry, physics and biology.

SUNBURN ERYTHEMA

There are two interesting features of burning red—the action spectrum and the energy exchange. There is a well-known maximum erythema at 297 mμ, and it would be convenient if this maximum were related to the absorption of a known compound in the skin which served as the initiator of the sunburn response. Unfortunately, no compound has been found capable of filling the required rôle. The only interpretation of *natural* sunburn which seems at all likely is to suppose that it is a complex response. It is then a resultant of activating and inhibiting reactions, each presumably with its appropriate wavelength maximum and a proportionate influence on the final result.

The energetic requirements of sunburn erythema have yielded interesting results by using tremendously high energy flashes as the stimulus. Photolysis flash lamps, such as are used in physicochemical studies, have provided the appropriate light source. By this means it has been established that by increasing the energy over a ten-millionfold range, reducing proportionately the duration of the light flash, a constant erythema can be provoked. Apart from changes due to the optical inhomogeneity of the skin, this finding supports the concept of an initially uncomplicated photolytic process. By these methods, the effects of inhibitors can also be usefully studied in the intact subject.

Measuring erythema responses has been until now a matter of measuring how much more red blood there is in the skin. Reflectance spectrophotometry is all one seems to need, at the proper wavelength, for oxyhaemoglobin. However, there is more to the physiology of sunburn redness than this, as the following case shows.

A patient with a psoriasiform eczematide recently developed a severe sunburn. He showed a marked white dermographism (blanching on stroking) on the areas of moderate sunburn which was absent in those more severely burnt parts. Unsunburnt areas showed the usual red reaction on stroking.

BLUE SKIN COLOUR

Dr. Oettlé and I have found ourselves engaged in friendly controversy on the origin of naturally occurring non-vascular blue tints in skin. My contribution was to say that the epidermis plays no part in causing blueness, and I have held that blueness results from the combined optical absorptive properties of collagen and a dark absorber such as melanin. Oettlé holds that blueness sometimes comes from collagen alone through an optical interference mechanism. There is a monkey in the Pretoria Zoo which may give Oettlé some fine support for his views. He is an albino and, despite this, the scrotum and parts of the chest show the same bluish tint that normally pigmented vervets display. If this monkey can be shown to have no dermal melanin either, knowing as we already do that he has no epidermal melanin, Oettlé's findings with the incident microscope will be neatly proved.

CHEMICAL STRUCTURE AND LIGHT REACTIONS

Light reactions can sometimes be clearly related to chemical compounds of known structure, and the molecular features can be definitely related to the reaction. Nevertheless, it is not easy to integrate these results into the mechanism of photo-reactions. Furocoumarins, for instance, cause an abnormal skin redness after exposure to long ultraviolet rays, and the chemical bonds and groups necessary for this are known. Similar 'families' of photo-active substances are known such as the phenothiazines and the para-amino grouping in sulphonamides and their derivatives (e.g. in oral antidiabetic drugs).

Several hypotheses have been used to explain hypersensitivity to light with these drugs, e.g. light speeds the oxidation of the drug to an allergenic breakdown product. Unfortunately, explanations of this sort are seldom much more than a display of scientific clichés derived from the advanced medicine of 50 years ago. A mid-century audience should not be prepared to listen to classifications based on physiological, toxic and allergic responses and believe that something useful has been said. In our section at Pretoria we have, for instance, only come across one photosensitive reaction to an oral antidiabetic drug. On theoretical grounds this should be similar to that caused by sulphonamides because of the para-amino grouping. However, in our patient's case this was not so, since she is light-sensitive only when taking methyl-substituted antidiabetic drugs and not to the para-amino series.

Regarding the porphyrins, their relation to photosensitivity must be closely linked to the forces of dermo-epidermal adhesion. The dermatologist must still humbly enquire if the chemist working on glue can help him, before he can decide how porphyria weakens the skin's adhesiveness on the parts exposed to light.

Certain abnormal light reactions can be controlled with antimalarials, and in the past 2 decades these drugs have proved their usefulness. Their mode of action has been the subject of all kinds of theories and investigations based on them. 'Conserving the level of ATP in the skin' is a theory that I worked on and discounted. Actions through light filtration and adrenal cortical stimulation are also apparently unworkable. The only view which seems tenable stresses the adsorption of antimalarials to nuclear material. The drugs then act protectively, limiting the lysis of DNA by light or other lytic influences. Perhaps the antimalarials act on the basic proteins (protamines and histones) which are thought to bind the DNA of the chromosomal units.

A promising field for investigating light reactions is the part played by organic free radicals. Free radicals have an unpaired electron in one of their molecular orbitals, and they are consequently highly reactive. They could stop or divert a chain reaction and probably are important in oxidation-reduction intermediates, both normal and abnormal in the body. The oxygen-dependence of some photoactivations may, for instance, be influenced by these free radicals. Moreover, melanin itself and certain metabolic products of the photosensitizer, chlorpromazine, are stable free radicals. This chemical property of melanin may, in fact, prove to be more significant than its importance as an absorber of light in protecting one from light reactions.

SUNLIGHT, DNA AND CANCER

It is known that ultraviolet light induces mutations in micro-organisms. Its ability to produce mutants in phages, sometimes by altering only one unit in a phage particle, suggests that some reactions of sunlight on the skin could take place by inducing a mutation in an epidermal cell. Such a mutant cell will through its descendants come to colonize a limited area of the skin surface. Burnet has suggested that this may explain the origin of solar keratoses. The same idea had also occurred to me, mainly because the lesions heal so well when the affected cells are killed off, and the skin regenerates from round about. If the same mechanism applies as it does with bacteriophage, the light is primarily active in deranging a part of the DNA spirals in the nucleus.

On the other hand, if cancer is the adaptation of cells to poorer nutritional supplies, we may have a way of accounting for the precancerous influence of senile elastosis. As a result of sun and exposure the upper dermis tends to lose its bundled, fibrillar structure and becomes more jelly-like. Possibly this layer may interfere with skin nutrition in the same way that experimentally inserted plastic membranes may do, which hamper the nutrition of the overlying cells and favour cancerization.

It seems unwise to under-rate the hereditary factor for variations in sun-induced skin cancer. Skin colour, if the free radical properties of melanin are of no importance, seems to me to be of little direct significance, as witnessed on the one hand by xeroderma pigmentosum and squamous carcinoma in the Bantu child,

and on the other by the failure of albino Bantus to develop rodent ulcer. In splitting up my own White patients with rodent ulcer according to age and sex, the sex incidence was equal up to 40 years, but men outnumbered women after that. Here I would like to imagine that hereditary or naevoid tendencies to rodent ulcer affect the sexes equally at earlier ages, but that more sun exposure in men gives them the lead when the environmental effects start showing in later life.

When the victim of skin cancer has a known genetic background, the influence of light can be studied in relative isolation. In this way, Blum has done a great deal on the production of cancers in the ears of genetically homogeneous albino mice with ultraviolet light. His forthcoming book on the subject promises much of interest, but here I shall discuss only the deductions made by him from the growth curves of the tumours as related to different amounts and methods of dosage with ultraviolet light. He concludes that ultraviolet carcinoma is not a threshold phenomenon, but a virtually irreversible cumulative process, and as the radiation continues there is a progressive acceleration effect on the ultimate carcinoma growth rate. I find Blum's speculations on the production of this growth pattern less appealing, and he seems not to allow for loss of volume in cell growth, maturation and death in the tumour. If these ideas can be transferred to Man, it would mean that the more ultraviolet there is on the skin, the sooner will cancer appear and the faster will it grow. The less light one gets, the slower to come and the less proliferative will the cancer be if it comes at all within one's lifetime.

LIGHT AND THE VITAMINS

The peculiar chemical structure of vitamin A is put to use in the retina for light perception where the organism possesses eye structures, but some primitive organisms may react to light with parts of their covering other than eyes or eye-spots. Vitamin A has an auxiliary function in skin keratinization of mammals, but its relation to cutaneous light sensitivity is still unexplored. Through the C.S.I.R. we propose investigating this question shortly.

Vitamin B complex deficiencies are classically related to the sun dermatitis of pellagra. We are busy with assays of co-enzymes 1 and 2, into which nicotinamide is built, to see how they behave in pellagrous subjects. Pantothenic acid and copper metabolism was the subject of earlier work by us (not too satisfactory, I fear), since pantothenic acid deficiency is related, in some species and possibly in Man, by raised tissue and blood copper levels. Copper and light are in turn connected by the necessity for bound copper in certain melanin-synthesising enzymes.

Pigmentation is inhibited by vitamin C as a reducing agent, but the main role of the vitamin in our own studies has been the observation that it is rapidly destroyed *in vivo,* in the presence of the ferric iron of iron storage disease in the Bantu.

Vitamin D in animals is formed by light from the provitamin, but it is only quite recently that the same mechanism has been shown to operate in Man. By gas chromatography the malpighian layer has been proven to contain enough provitamin to produce sufficient vitamin D by sunlight conversion. The use of ultraviolet light for lupus vulgaris is thought to depend for its claimed successes on this conversion.

PHOTOPERIODISM

Although only indirectly connected with skin reactions to light, the concepts of photoperiodism have considerable importance and interest.

In the chemical sense, photoperiods are important in studying chain reactions in the gaseous state. If the illumination initiating a complex reaction be applied continuously, a constant proportion of intermediates is soon reached. If, however, the light is alternated with periods of darkness, different reaction patterns will emerge. In plants a similar situation applies, and flowering may be initiated merely by a certain rate of change of the ratio between day and night length. In man, the influence of the photoperiod is not immediately evident, whatever poets may have to say about the springtime. Nonetheless, there are 3 changes in mammalian skin which are probably influenced by alternating periods of darkness and light. One is the diurnal mitotic rhythm of the epidermis; another is the seasonal moulting with possible change of coat colour in certain mammals; and the third is seasonal skin disease in Man.

My friend, Dr. Alice Carleton of Oxford, studied the epidermal mitotic rhythms in animals some 25 years ago, and established that mitoses were most plentiful at night. This rhythm was made chaotic by keeping on an electric light all the time. Zola Cooper later showed that *covered* areas of skin in Man showed a diurnal mitotic rhythm as well, when all other factors such as age, sex, temperature and humidity were excluded, and light cycles

were the only changing feature of the environment.

Seasonal moulting in fur-covered mammals is widespread and, in addition, certain Arctic species have different coloured coats in summer and winter. It seems that mammals which moult with or without a change of coat colour do so as a result only of changes in the duration of the light stimulus.

Since these responses in the skin take place whether the skin is covered or not by fur or clothing, the receptor of light must surely be the eye, whether closed or open. The pituitary has been supposed to be the outflow pathway of these brain stimuli, but other ways are not excluded.

When a disease of the skin affects humans seasonally, no attempts have been made so far to see whether these changes have anything to do with lengthening photoperiods. Most of the seasonal dermatoses start in spring (September—October in this country) and the plant world is usually given the blame—green fruit, pollens, and what not. Even if some seasonal dematoses are traceable to seasonal allergens, increasing day length may provoke the genetically determined tendency to develop the complaint in question.

It seems as if we are back in a jungle of primaeval behaviour patterns, in which a banal stimulus like light can affect the operation of some characteristic living rhythms. The ability of the organism to respond is a genetic affair, and involves functional conditioning at the higher levels of the central nervous system.

I believe that modern journalists have discovered a law which decrees that there must only be one single thought for every 5,000 words written or spoken. Now, having disobeyed this valuable precept, I feel it is only proper to close the subject of the skin and light before any second thoughts occur to me.

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PEPTIC ULCER IN INDIANS AND AFRICANS IN NATAL

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Recognizing the importance of diet and certain psychosomatic factors as contributory causes in the development of peptic ulcer, it was decided to review the cases of this disease treated at Edendale Non-European Hospital over the past 4½ years. By comparing the incidence of the disease in the 2 racial groups served by this hospital, and by correlating it with such factors as diet, residence and employment, it was hoped to obtain an indication of the importance of these factors. For contrast with the established picture of this disease in White patients, a review of the symptomatology, physical findings, incidence of complications and response to treatment was also undertaken.

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Edendale Hospital, with 750 beds, serves the Indian and African communities of Pietermaritzburg and the Natal Midlands and receives referred cases from several surrounding hospitals and from Northern Natal. Therefore as regards residence, the patients are derived from both urban and rural areas, and represent a fair cross-section of these 2 racial groups in this part of Natal Province.

During the period under review 102 cases, reliably diagnosed as peptic ulcer, were seen. These form the basis of this discusion. During the same period 3 cases of gastric perforation due to fungus infection, in malnourished infants, were observed.[8, 12] These are not included for the purpose of this discussion.

DISCUSSION

INCIDENCE

In the period under review the total hospital admissions, excluding maternity admissions, numbered 44,771 cases. Of this number 40,209 were Africans and 4,562 Indians. Of the total number of peptic ulcer cases, 58 were African and 44 Indian patients. Thus, of every 1,000 African admissions, 1.44 were for peptic ulcer, whereas this figure for Indians was 9.64, or 7 times greater.

It is interesting to compare this with the incidence of gastric carcinoma in the 2 races. During the same period there were 30 cases of carcinoma of the stomach amongst the Africans (an incidence of 0.75 per 1,000 admissions) while there were only 2 Indian cases (0.44 per 1,000 admissions).

AGE AND SEX INCIDENCE

Table 1 shows the age distribution for male and female patients of both groups. There is close agreement in that in both groups the largest incidence is in the age group 20–50 years (82% of the total number) while 60% of the total number occurred in the age group 20–40 years. This last figure is almost the same as that given by McKenzie.[10] A significant number of cases occurred in the age group 10–15 years.

Case 1. V. N., an African male of 13 years, was admitted with a 2-year history of recurrent abdominal pain unrelated to meals, and vomiting. There was no loss of appetite or of weight. The patient appeared healthy, and moderate tenderness and some guarding in the epigastrium were the only physical findings. The haemoglobin level was 13 g. % and the sedimentation rate 23 mm. for the first hour. A barium meal examination revealed a clear-cut, unequivocal duodenal ulcer crater.

After treatment for a month on a conservative regime, all symptoms had disappeared and the patient was discharged. When seen again 3 months later, the symptoms had recurred. A further barium meal showed the duodenal ulcer as before, with a 'pre-stenotic' diverticulum. He again improved on medical treatment and was discharged a month later.

Case 2. P. D., an Indian scholar aged 14 years was admitted to hospital with the complaint of recurrent epigastric pain for 2 years. The pain came on 1–2 hours after meals and was relieved by taking milk or food. His diet consisted chiefly of curry, rice and bread. His appetite was good.

The patient was in severe pain. Deep epigastric tenderness was present but no rigidity. Bowel sounds were present and the findings on rectal examination were normal. Barium meal examination showed a clear-cut ulcer crater in the duodenal cap.

The pain disappeared after medical treatment.

Case 3. K. P., an Indian male scholar aged 15 years, gave a history that for the past 3 years he had suffered from hunger pains in the epigastrium, coming on 2 hours after meals. The pain was relieved by taking milk or bananas. Taking 'hot' foods (e.g. curry) was often associated with salivation, abdominal pain, nausea and vomiting. The pain often woke him at night. His diet consisted mainly of curried foods. His brother, aged 18 years, also complained of similar symptoms.

Two weeks before admission the patient passed a black stool. A week later the epigastric pain became sharp and radiated to the umbilicus and lower abdomen. About 6 hours before admission the pain became very severe.

On examination he appeared distressed and in considerable pain. The tongue was furred, pulse rate 88 beats per minute and the blood pressure 110/60 mm. Hg. There was extreme generalized abdominal tenderness and rigidity and a positive release sign. There were no audible bowel sounds and rectal examination showed marked tenderness in the recto-vesical pouch.

TABLE 1: AGE DISTRIBUTION OF MALE AND FEMALE PATIENTS OF BOTH POPULATION GROUPS

Group		*Age (Years)*					
		10—20	*20—30*	*30—40*	*40—50*	*50—60*	*Over 60*
Indian	Male	3	14	10	8	4	1
	Female	—	1	1	2	—	1
African	Male	3	13	13	12	6	3
	Female	—	2	5	—	—	1

Laparotomy revealed an odourless, bile-stained peritoneal fluid, a normal appendix and a 4 mm. perforation in the anterior wall of the first part of the duodenum. The defect was closed. The post-operative course was smooth and the patient was discharged on the tenth day on a light ulcer diet with alkalis and sedatives.

Two months later a barium meal examination showed gross distortion of the duodenal cap. The emptying time of the stomach was normal. He had had occasional mild attacks of pain. Treatment as an out-patient was continued.

It is also evident from Table 1 that there is a much higher incidence of peptic ulcer amongst the male members of both groups. The total number of male and female admissions for the period under review was nearly equal. In the Indian group, the females formed 11% of the total number of cases, while there were 6 female African cases (11%)—a ratio of 9:1.

In Table 2 the cases are analysed according to the situation of the ulcer in the 2 sexes; the only significant feature is the clear male preponderance in the gastric ulcer group in the African.

TABLE 2: SITUATION OF THE ULCER IN BOTH SEXES OF THE TWO POPULATION GROUPS

Group		*Duodenal*	*Gastric*
Indian	Male	34	5
	Female	4	1
African	Male	39	10
	Female	5	1

In contrast with the sex incidence for peptic ulcer, it is again interesting to note that, in the gastric carcinoma group, the proportion of African females is much higher: 11 of the 30 cases were females (36.6%)—a ratio of more than 1:3 as compared to 1:9 in the peptic ulcer group. What part, if any, such factors as malnutrition, avitaminosis and the consumption of home-made alcoholic concoctions (to which both sexes are partial) may play in the causation of gastric carcinoma or peptic ulceration, is open to speculation. If there is any relationship, such factors appear to produce a dissimilar response in the 2 sexes.

INCIDENCE CORRELATED WITH RESIDENCE, DIET AND EMPLOYMENT

These 3 factors are so intimately associated that no attempt will be made to treat them individually.

From this point of view, the Indian cases form a reasonably uniform group. They are mostly semi-skilled or skilled workers, business people, and a fair proportion from the professional classes. Most of this group is resident in the towns or in the larger villages, while a small number are from farming areas (market gardeners and fruit growers) near the towns. They all consume a similar type of diet reasonably varied but with the 'hot' foods (curried and spiced preparations) as important constituents. The members of this group, as a whole, tend to be of the worrying, introspective type, with a lower tolerance to pain than the African. They are subject to the stresses of modern civilization to the same extent as the European.

In this group the incidence of peptic ulceration is much higher than in the African group. The importance of diet in relation to this high incidence is uncertain; undoubtedly most patients volunteer the information that the taking of spiced foods regularly aggravates their symptoms Later it will be shown that the incidence of perforation is also higher in this group.

The African patients could be subdivided into 2 broad groups on the basis of residence, diet and work. The first group includes those patients living and working in the towns and villages and on the farms. The great majority of these are unskilled or semi-skilled workers, while a small number are clerks, teachers, policemen and nurses. The diet is varied and tends, as far as purchasing power permits, to approach the European diet. The system of rations on the farms, the availability of farm produce to the workers and the consumption of the overflow from the European kitchen, bring the diet of the farm labourers into the same class as that of the town resident. This group, because of its contact with the rush of civilized existence, competing on the open labour market, often living away from their wives and families, and their contact with modern industry, probably suffers from the stresses, inseparable from modern civilization, a good deal more than those in the next group.

The second group is made up of patients from the Reserves. Here, life still proceeds, more or less, along the established tribal ways, with the women doing a considerable part of the work required for the cultivation of the small farms and the fetching of fire-wood and water. The diet consists chiefly of mealie meal, with meat on occasions and milk during certain times of the year. Vegetables and fruit are only rarely available and beverages are

normally not taken. The food supply depends on the yield of the land and on the rainfall. Towards the end of a severe winter the patients are generally poorly nourished, especially the smaller children and the very old. Home-brewed malts are regularly taken by the men, and these are probably purer than the intoxicating preparations available, often illegally, in the town locations.

Of the African peptic ulcer cases it was possible to ascertain their place of residence sufficiently accurately in 46 cases. Only 3 cases were from the Reserves, and the rest could be classified into group 1 above. It is not possible to express this correlation statistically because it is not known what percentage of the total number of hospital admissions comes from the Reserves. It can, however, be accepted that the patients in group 1 show a definitely increased incidence of peptic ulceration.

The nature of the work could be ascertained in 33 of the African cases. All of these were in group 1.

SYMPTOMATOLOGY

Duration of Symptoms. The most outstanding feature was the short duration of symptoms in the African cases. This is especially important in those cases presenting with perforation. The diagnosis of a perforated ulcer should not be discarded because of the absence of previous ulcer symptoms.

Case 4. M. K., an African female aged 30 years, gave a 3-day history of vague, right-sided abdominal pain, with nausea and loss of appetite. Six hours before admission the pain had suddenly become severe and cramp-like, more severe in the upper abdomen and referred to the shoulder tips. She vomited copiously. Her last menstrual period had started 5 days before admission. She had some vaginal bleeding again following the onset of the severe abdominal pain.

She showed marked mucosal pallor, the pulse rate was 110 beats per minute, and the blood pressure 100/65 mm. Hg. There was slight generalized abdominal distention with tenderness, guarding and signs of free fluid. Bowel sounds were absent. Vaginal examination revealed tenderness in the fornices and adnexae and a mass could be felt in the anterior fornix. The haemoglobin level was 7.2 g. %.

A diagnosis of ruptured tubal gestation was made. At laparotomy a milky fluid was present in the abdominal cavity. The uterus contained several fibromyomata. The adnexae were normal. At the pyloro-duodenal junction there was a perforated ulcer on the posterior aspect. This was closed.

The post-operative course was normal and the patient was discharged and advised to take an ulcer diet.

Eight African cases gave histories of a duration of symptoms before admission of hours or days, while in 36 the period was weeks or months. Thus, where the Indian patient will mostly present with symptoms for a year or more, the African usually gives the duration in days or months.

There is often indirect evidence that the patient's story may not be reliable, e.g. evidence of repeated scarification as is used by the 'medicine man' over the area where the pain is localized. Again, having to take the histories through an interpreter probably makes them less accurate than a detailed direct interrogation.

Case 5. E. K., an African female aged 26 years, was admitted complaining of upper abdominal pain for one year. The pain was continuous, at times severe, and came on during or just after meals. There was frequent vomiting of food just taken. She had lost a considerable amount of weight. She had noticed that her abdomen had become distended.

There was central epigastric abdominal distention and a rounded, mobile, firm and slightly tender tumour could be felt in the epigastrium. The haemoglobin level was 11.1 g. %. A barium meal examination showed a large stomach, obstructed at the pylorus. A gastric neoplasm was considered the most likely diagnosis.

At laparotomy a large chronic ulcer was found in the first part of the duodenum. Partial gastrectomy was performed. The post-operative course was satisfactory.

SYMPTOMS AND SIGNS

The most common presenting symptom was upper abdominal pain. This was present in 97% of the Indian patients and in 91% of the African group. A third of the Indian cases noted periodicity of the pain whereas in only 13% of the Africans was this noted. Vomiting, haematemesis, melaena and loss of weight were all more frequent in the African patients whereas the Indian patients experienced loss of appetite more frequently. Two African females were pregnant when the diagnosis of duodenal ulcer was first made.

In the uncomplicated cases, the most constant physical sign was a rather ill-defined tenderness in the epigastrium, present in slightly more than half of the patients in each group.

In 54 cases (22 Indian and 32 African) the diagnosis was confirmed by the demonstration of an ulcer crater in the duodenum (37 cases) or stomach (17 cases) on barium meal examination. In a further 36 cases (15 Indian and 21 African) the barium meal revealed definite deformity of the region of the duodenal cap, while tenderness, localized to this area, could be demonstrated on screening. These findings, in a patient presenting with symptoms and

signs suggestive of peptic ulcer, were accepted as confirming the diagnosis. The diagnosis in certain cases of this group was later established at operation.

INCIDENCE OF COMPLICATIONS

The occurrence of haematemesis in 35 cases (8 Indian and 27 African) and melaena in 25 cases (9 Indian and 16 African) has already been mentioned. These figures are analysed in Table 3. Really alarming haemorrhage occurred in only 2 cases, both African.

TABLE 3: INCIDENCE OF COMPLICATIONS IN DUODENAL AND GASTRIC ULCER CASES IN THE TWO POPULATION GROUPS

Group		*Perforation*		*Haematemesis*		*Melaena*	
		Duodenal	*Gastric*	*Duodenal*	*Gastric*	*Duodenal*	*Gastric*
Indian	Male	7	4	6	—	7	1
	Female	—	—	2	—	1	—
African	Male	1	2	19	3	13	—
	Female	1	—	4	1	3	—

Case 6. G. D., an African male aged 27 years, complained of abdominal pain for 3 days. He was admitted after a severe haematemesis. As bleeding recurred on medical management, a laparotomy was performed. No evidence of gastric or duodenal ulcer could be found. A partial gastrectomy was performed, and on detailed examination of the specimen a superficial erosion on the gastric mucosa was found. He recovered.

Case 7. A. R., an African male aged 32 years, was admitted complaining of abdominal pain for 3 weeks and marked increased frequency of urination for one day. He had a pelvic abscess and a large walled-off cavity under the left lobe of the liver, communicating with a perforation on the lesser curvature of the stomach. The perforation was closed and the subhepatic and pelvic abscess cavities drained. On the eighth post-operative day he suddenly had a severe haematemesis. Laparotomy disclosed a large duodenal ulcer, completely encircling the first part of the duodenum, with active bleeding from a vessel on the surface of the pancreas. The patient died 3 days after the operation.

The incidence of perforation in this series is also shown in Table 3. It is noticeable that perforation was a much more frequent event in the Indian group, where one of every 4 patients presented with this complication, as compared with only one in 14 in the African group of 58 cases.

Another feature in the perforated cases was that admission in the Indian cases was almost always within hours after the onset of acute symptoms, whereas the admission of the African cases tended to be much later. Case 7 illustrates this point. This delay could not be explained as due to lack of transport, remoteness from the hospital or delay in making the diagnosis.

It would appear that the peptic ulcer bleeds more often in the African patient and perforates more frequently in the Indian.

TREATMENT AND RESPONSE

Excluding patients presenting with obstruction or perforation, all cases were initially treated conservatively on a regime of rest, diet, alkalis (magnesium trisilicate and magnesium hydroxide), sedatives and a parasympatholytic drug. Of 78 patients treated in this way, 56 (19 Indian and 37 African) improved to the extent that all their symptoms disappeared while in hospital. In 22 cases (11 Indian and 11 African) there was either failure to improve initially or symptoms recurred following conservative treatment.

Operative treatment was always preferred when the diagnosis of a perforated ulcer was made. This consisted of simple closure of the perforation in 13 cases, partial gastrectomy in one case, and in one patient, where a previously perforated gastric ulcer was found to have sealed off, the lesion was left undisturbed. In one patient (an Indian) a second perforation occurred and was closed.

In patients who presented with obstruction or where symptoms recurred after thorough, conservative treatment or after simple closure of a perforation, partial gastrectomy was the treatment of choice. The operation was performed in 20 cases (6 Indian and 14 African). The Polya-Hofmeister technique with an anterior loop was used in 19 cases and one patient had a Billroth I type resection. Two male African patients with long-standing

pyloric obstruction and a low acid secretion had a gastroenterostomy performed.

The operations were well tolerated in all cases. Three Indian patients and one African female complained of some epigastric discomfort after big meals post-operatively. One African male developed a mild but definite dumping syndrome. In no case was there any suggestion of the development of a stomal ulcer.

In the entire series, over the period of hospitalization and observation in the Out-Patient Clinic, there was only one death (Case 7).

SUMMARY

A review is presented of a group of 102 cases of peptic ulcer treated at the Edendale Hospital over a period of 4½ years. Of this group 44 were Indians (an incidence of 9.64 per 1,000 admissions) and 58 African (1.44 per 1,000 admissions).

An attempt is made to correlate the incidence of the disease with the place of residence, diet and work of the patient. It would appear that the incidence of peptic ulcer is much higher in the urbanized African.

The age of maximum incidence is lower, in both Indian and African groups, than in White patients.

Symptoms are often apparently of short duration in the African patient in spite of the presence, radiologically and pathologically, of a chronic ulcer.

Bleeding from a peptic ulcer is more common in the African than in the Indian patient, while the reverse is true for perforation.

Response to treatment, conservative and operative, is satisfactory.

This paper is submitted for publication with the kind permission of the Director of Medical Services, Natal.

We wish to thank Dr. T. N. Adnams, Medical Superintendent, Edendale Hospital, for his permission to consult the records.

We are indebted to Dr. W. R. Phillipps, Head of the Division of Surgery, Edendale Hospital, for his interest in this study.

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TRANQUILLIZERS AND PSYCHO-ENERGIZERS

LEWIS A. HURST, B.A., B.SC., M.B., CH.B., PH.D., (C.T.) M.D. (PRET.)*

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In this review I shall attempt an evaluation of the two groups of psychotropic drugs, the tranquillizers and psycho-energizers with their revolutionary implications both for the aetiology and therapy of certain psychiatric conditions. A constant critical evaluation of this rapidly expanding field is important not only to the specialist but also to the general practitioner who, by and large, handles a greater number of patients who stand to benefit by such treatment.

I. THE TRANQUILLIZERS

A new era in psychopharmacotherapy was inaugurated by the laboratory work which gave us the phenothiazine and rauwolfia derivatives, the former of which have captured the field and will absorb our attention exclusively.

Several phenothiazine derivatives have been evolved by changing the halogen attached to the nucleus or by varying the configuration of the side chain. Examples of the halogen moieties are the chlorine, methyl, methoxy, acetyl and trifluoromethyl ones. Variants of the side chains are short and long, and those with a piperazine or a piperidine ring in them. Upon these features the potency, safety and toxicity of the individual product depend.

Extensive clinical trials, on ambulatory and hospitalized patients, for periods of from a few weeks to 5 years, too numerous to instance in a general article of this kind, are on record. Thus a report by Ayd (1959),[1] concerned a group of over 4,000. Many studies establish a control by means of the 'double blind'

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method, and thus improve the scientific reliability of their conclusions.

New phenothiazine drugs are rapidly appearing; hence the need for vigilance and frequent readjustment on the part of the medical profession.

GROUPING OF PHENOTHIAZINE DERIVATIVES ON THE BASIS OF CHEMICAL STRUCTURE

Phenothiazine derivatives fall into the following 3 groups on the basis of chemical structure*:

1. The *piperazine* group, characterized by a piperazine ring in the side chain, represented by Trilafon (perphenazine), Stelazine (trifluoperazine) and Permitil or SCH6894 (fluphenazine).
2. The *chlorpromazine model* group, characterized piperazine ring in the side chain, represented by Largactil or Thorazine (chlorpromazine), Vesprin (triflupromazine), Sparine (promazine) and Tentone (methyoxypromazine).
3. The *piperidine* group, characterized by a piperidine ring in the side chain and represented by Pacatal (mepazine).

POTENCY AND SIDE EFFECTS

The features of clinical bearing in respect of these drugs to which I shall limit this review are: (*a*) potency and (*b*) side effects.

(*a*) *Potency*: The criteria upon which these assessments are made are: level of psychomotor inhibition achieved, speed of action and the effective dosage.

By these standards, Pacatal and Sparine are half as potent as Largactil, while Trilafon is 5 times, Stelazine 8 to 12 times and Permitil 10 to 20 times as potent.

The relative potencies of the phenothiazine compounds are related to chemical structure.

Pacatal, which does not contain a side chain with 3 carbons, is the least potent phenothiazine derivative. Sparine and Tentone have a 3-carbon straight chain and are approximately equipotent. They are, however, the least potent members of the chlorpromazine model group. The importance of the halogen attached to the nucleus is exemplified by Largactil and Vesprin. The chlorine halogen endows Largactil with twice the potency of Sparine and Tentone. The trifluoromethyl halogen gives Vesprin 1.5–3 times the potency of Largactil. Moreover, the addition of the piperazine ring to the side chain renders all the members of this group more potent than the chlorpromazine model drugs. That the halogen joined to the nucleus is as important as the piperazine ring in the side chain is illustrated by an experimental piperazine derivative which does not have a chlorine or trifluoromethyl halogen and which accordingly diminishes its potency to that of Largactil.

(*b*) *Side Effects*: These include a variety of autonomic, endocrine, dermatological, hepatic, haematopoietic and neurological reactions which are related to potency and chemical structure.

Autonomic side reactions are most prominent with the weaker derivatives, Pacatal, Sparine and Tentone.

Ascending the potency scale from the piperidine to the piperazine group there is a progressive decrease in *endocrine* effects. The most prominent endocrine effects occur with Largactil and include polyphagia, polydipsia and polyuria, weight gain and altered menses and lactation.

Dermatitis, jaundice and agranulocytosis have been classified as *allergic* reactions to phenothiazine drugs.

While *allergic skin* reactions are widespread they are more frequent with the weaker derivatives and rare with members of the piperazine group.

Jaundice likewise is rare in the piperazine group, while chlorpromazine and Pacatal show the highest incidence. Chlorpromazine jaundice has been the subject of intensive study because of raising the question of potential adverse effects on the liver. The outcome has been to demonstrate that even large doses administered over 2–4 years have no deleterious effect on the liver as assessed by several liver function tests.

Agranulocytosis has been caused by all piperidine and chlorpromazine model drugs except Tentone, but not by the piperazine group. Most blood dyscrasias have occurred in the first 4 months of therapy, and adequate studies have shown that prolonged administration of the drugs in question is most unlikely to have adverse effects on the haematopoietic system.

* Some of the available preparations in South Africa are:

Benzedrine (Smith, Kline and French Laboratories Ltd, SKF Laboratories (Pty.) Ltd.).
Dexedrine (Smith, Kline and French Laboratories Ltd, SKF Laboratories (Pty.) Ltd.).
Largactil (Maybaker (S.A.) (Pty.) Ltd.).
Marsilid (Roche Products (Pty.) Ltd.).
Nardil (Warner Pharmaceuticals (Pty.) Ltd.).
Niamid (Pfizer Laboratories (Pty.) Ltd.).
Pacatal (Wyeth Laboratories (Pty.) Ltd.).
Permitil (White Laboratories, Inc.).
Ritalin (Ciba (Pty.) Ltd.).
Sparine (Wyeth Laboratories (Pty.) Ltd.).
Stelazine (Smith, Kline and French Laboratories Ltd, SKF Laboratories (Pty.) Ltd.).
Tofranil (Geigy South Africa (Pty.) Ltd.).
Trilafon (Schering Corporation).

Seizures occur as side effects with increasing frequency as one descends the potency scale of the chlorpromazine model and piperidine groups. Sparine and Pacatal have caused the highest incidence of seizures, but even with them the figure is low.

Extra-pyramidal reactions are of common occurrence with these drugs. They include akinesia (weakness and muscular fatigue), dystonic reactions (retrocollis, torticollis, facial grimacing and distortions, dysarthria, laboured breathing and involuntary muscle movements and oculogyric crises), and akathisia (motor restlessness). These extrapyramidal manifestations are to be regarded as totally reversible drug effects, which may be eliminated by reduction of dosage, mild sedation or anti-parkinsonian drugs (2 mg. Cogentin or Akineton intramuscularly). They occur with increasing frequency, appear earlier in time and with progressively smaller doses of the drug as one ascends the potency scale from the piperidine to the piperazine group. But it has also been shown that extrapyramidal reactions are more a matter of individual susceptibility than of chemical structure, potency, dosage, or duration of treatment.

MODE OF ACTION OF PHENOTHIAZINE DERIVATIVES

With Special Reference to *Sites of Action in the Central Nervous System*

Although there is clinical evidence to suggest that phenothiazine derivatives have widespread action in the body, the following considerations suggest that they act primarily on 3 neuro-anatomical systems—the reticular system of the medulla, mid-brain and diencephalon; the hypothalamus; and the limbic system, especially the amygdala and hippocampus:

1. The anti-emetic action of these drugs, which implies depression of the medullary reticular formation.

2. The capacity of some members of the series to potentiate barbiturates and to sedate, which suggests an effect on the mesencephalic reticular system and hypothalmic structures.

3. The autonomic and endocrine effects of these drugs, which indicate the hypothalamus as the chemoreceptor site.

4. The extrapyramidal reactions caused by these drugs which point to an action upon the limbic system, especially upon the nuclei of the extrapyramidal system.

The relative selectivity of action of different members of the phenothiazine series on the 3 neuro-anatomical systems referred to, while adding to the rationale of the mode and sites of action of these drugs, provides specific indications for their therapeutic use.

Thus the weaker the phenothiazine compound (Pacatal, Sparine, Tentone and Largactil), the smaller its effect on the limbic system, the more effect it has on the hypothalamus and the greater its effect on parts of the reticular system. Conversely, the more potent the phenothiazine derivative (Permitil, Stelazine, Trilafon), the greater is its effect on the limbic system as its propensity to cause extrapyramidal symptoms suggests, and the less its effect on the hypothalamus and the reticular systems, as evidenced by its relative freedom from induction of drowsiness, autonomic and endocrine effects and depressive drug potentiation. Apart from these generalizations, an example of the sort of therapeutic consideration that emerges is the following: if sedation as well as tranquillization is required, as in acute excited states, Largactil or Vesprin would be the drug of choice; but where sedation is undesirable, as is frequently the case in ambulatory patients, Permitil, Stelazine and Trilafon would be indicated.

PRACTICAL CONSIDERATIONS IN THE USE OF PHENOTHIAZINE DERIVATIVES

The phenothiazine drugs are not curative. They nevertheless provide symptom amelioration which assists patients to adjust socially, live at home and quite often achieve some vocational adjustment.

The continuous administration necessary raises questions concerning the possible effects of long-term therapy—those of tolerance, addiction, and damage to liver, bone marrow and kidney. Clinical and laboratory evidence is favourable on all these points and shows specifically that protracted treatment with these drugs is without deleterious effects on liver, bone marrow or kidney.

With regard to the physician's choice of a phenothiazine drug, we have already referred to discrimination on the basis of the desirability of the presence or absence of sedative effects.

Probably the most general criterion guiding the physician is that he must choose a drug which will produce a satisfactory remission as quickly as possible with the least risk. For this reason the newer piperazine phenothiazine tranquillizers, notably Permitil and Stelazine, represent an advance over their predecessors for with their higher therapeutic response goes a lower incidence of neurological manifestations and a complete absence of other major

side effects, such as jaundice and agranulocytosis.

In conclusion, as a guide to the use of these drugs in practice, including an indication of the clinical conditions for which they may be employed, Table 1 (of the effective initial daily dosage range) is subjoined. Initial dosage is individualized according to the symptoms such as anxiety, tension and psychomotor excitement, and maintenance dosages are determined by individual requirements. It will be noted that the dosages employed in the case of psychoneurotic and senile patients are strikingly lower than in the case of the constitutional psychoses, schizophrenia and manic-depressive psychosis.

TABLE 1: EFFECTIVE INITIAL DAILY DOSAGE RANGE OF PHENOTHIAZINE DERIVATIVES (in milligrammes)

	Permitil	*Stelazine*	*Trilafon*	*Vesprin*	*Largactil*	*Sparine*	*Tentone*	*Pacatal*
Schizophrenia	2—10	10—60	32—64	100—300	300—800	500—1,000	500—1,000	500—1,000
Manic-Depressive Psychosis	10—20	20—80	32—96	200—400	300—1,200	500—1,500	500—1,500	500—1,500
Senile Psychoses	1—5	2—8	4—12	30—75	30—100	50—150	50—150	50—150
Psycho-Neuroses	1—5	4—20	8—24	30—150	100—300	150—400	150—400	150—400

II. THE PSYCHO-ENERGIZERS OR ANTI-DEPRESSANTS

The *amphetamines* (Benzedrine, Dexedrine), which are to be classified as CNS stimulants, have for many years enjoyed a vogue in the ambulatory treatment of mild depressive states, in which the more severe treatment of electro-convulsive therapy often entailing hospitalization is considered not quite justified. Such treatment has been found of value in tiding patients over short-lived depressive episodes of 2 or 3 weeks' duration. Many physicians and psychiatrists prefer administering these drugs in combination with a barbiturate (e.g. in the form of Drinamyl) to counteract the tendency of amphetamines to produce insomnia. A spansule form of Dexedrine has been produced to achieve prolonged and steady absorption throughout the day. Benzedrine and Dexedrine, because of their property of increasing vigilance and intellectual productivity, have also achieved popularity among students prior to examinations, and among motorists doing night driving to stave off sleep. Experimentation in Eysenck's laboratory[2] has proved that the impression of enhanced vigilance and mental productivity under this drug is not merely subjective but also substantiated by objective measures. Tofranil is also an anti-depressant that is gaining in popularity. The details of its mood-regulating or thymoleptic action are still under discussion.

THE MONO-AMINE-OXIDASE INHIBITORS

These have recently attracted attention as anti-depressant drugs and bid fair to play a much more substantial, fundamental and long-term role in the treatment of depression.

The forerunner drug in this field was iproniazid, used in anti-tubercular activity. This drug was so widely accompanied by untoward side effects in its use in tuberculosis that in America it did not receive FDA approval. In 1956, however, the 'side effects' that had resulted in the discontinuation of the use of the drug led to its therapeutic use in depression. Its employment in the treatment of depression (marketed in the form of Marsilid) have revealed the points of contrast with the amphetamines listed in Table 2.

Despite the advance constituted by Marsilid, certain undesirable side effects indicated the need for a search for an allied but improved product. These *side effects* include orthostatic hypotension, acute liver damage (80 fatalities described in the United States), oedema, increase of urea nitrogen, increase of icteric index, anaemia and thrombocytopaenia, dermatoses, dizziness, headaches, hypoglycaemia, hyper-reflexia and increased muscle tone, insomnia, impotence and frigidity, constipation, difficulty in starting micturition, colour blindness and decalcification of bone.

With this formidable array of adverse side effects it is welcome news that in Niamid, Pfizer has produced an effective anti-depressant singularly free from them.

Niamid (Pfizer brand of nialamide). It is to this drug that I would now direct detailed attention. It has been submitted to extensive clinical trials and has been the subject of a

medical conference in Johannesburg in October 1959 and of an international medical conference at Lisbon in November 1959, under the auspices of the Society of Medical Sciences of Lisbon. As a participant in both conferences, I am in a position to give my impressions of salient findings concerning this drug.

TABLE 2:

Marsilid	*Amphetamines*
Inhibition of mono-amine oxidase which normally destroys adrenaline, nor-adrenaline and serotonin in the brain as well as in the liver and other tissues.	They are rapidly destroyed in the body, hence their action is not prolonged.
Produces a prolonged central stimulation which is not followed by a depressive phase.	Their effects tend to diminish on repeated administration, therefore requiring progressively larger doses. They are also habit-forming to some extent.
Tends to lower blood pressure rather than to increase it, particularly in the upright position.	Their stimulating action is usually followed by a depressive phase, which is a highly undesirable side effect.
Stimulates the appetite.	They decrease the appetite.
Very slowly metabolized in the body.	They tend to increase the blood pressure and the heart rate.

South African Experience: Johannesburg Conference, October 1959. The figures and broad picture from the combined experience of Henning, Lowenstein, van Wyk, Ginsburg and Gillis are as follows:

Among the 17 schizophrenics treated there was no significant improvement. In marked contrast to this, of the 16 endogenous depressions, 13 showed substantial improvement and in the 3 other cases it was too early to say. In 4 cases of reactive depression there was an initial release of anxiety suggesting a psychocathartic action of the drug. In one case of epilepsy there was a reduction in the incidence of seizures but no claim as to the statistical significance can be made. Two dosage schemes were employed—a gradual one commencing with 25 mg. thrice daily rising to 100 mg. thrice daily on the 18th day, and a more intensive one commencing at 50 mg. twice daily rising to 100 mg. 4 times daily on the fourth day. With the gradual scheme the beneficial effects on depression were only clearly detectable 14–21 days after the institution of treatment, whereas with the intensive plan such improvement was detectable as early as on the third day.

No serious or unpleasant side effects were recorded. Even insomnia was absent in patients receiving their last dose as late as 9 p.m.

The types of treatment upon which cases had been before their successful treatment with Niamid included the tranquillizers Largactil, Stelazine and Trilafon, the euphoriants Ritalin, Nardil and Tofranil, and also electro-convulsive therapy.

World Experience: Lisbon Conference, November 1959. The Lisbon Conference was widely international in its representation, delegates coming from the North and South American continents, Britain, leading continental countries and South Africa. Clinical and pharmacological aspects were extensively covered.[3]

A. CLINICAL ASPECTS

1. *Psychoses and Psychonoeuroses.* Papers were read in this section by Nistri and Scambati (Florence), E. Beresford Davies (Cambridge), Alanen and Toivakka (Finland), Mendes and do Rosario (Lisbon), Coirault, Janet and Desclos (Paris), Salera (the Argentine), Van Herck (Belgium), Van Reeth (Belgium), Hacquard and Balland (Nancy), Anderson (Rome) and Hurst (South Africa).

General features only can be described, as follows:

(*a*) *Indications*: Endogenous depressions including the involutional depressions responded well, reactive depressions usually not as well, schizophrenics at most symptomatically and with activation of delusions and hallucinations as well as of behaviour.

(*b*) *Dosage*: Optimal dosage was claimed to lie at varying levels from 75 to 300 mg. per day, a gradual mode of induction being generally favoured.

(*c*) *Interval before Clinical Response:* While some observers reported response on the first, third and fourth days, the general impression was that 8–14 days was a more representative period. Accepting this more conservative estimate, it is clear that in the acute depressions, especially those with suicidal indications, it is necessary to combine Niamid with some other form of treatment, notably ECT. The Parisian workers claimed that increasing age was associated with delayed clinical response.

(*d*) *Side Effects*: The consensus of opinion is that Niamid is free of serious side effects.

Van Herck, in a masterly paper, made the following generalization in line with the general experience: Nialamide is a potent, non-toxic thymoleptic, valuable in endogenous depression, but without effect in schizophrenia. It has decided advantages over Marsilid in the absence of the side effects constipation, hypotension, impotence and frigidity, weight change, polyneuritis and sphincter disorders.

2. *Mental Retardation.* Rett (Vienna) claimed behavioral improvement, and de Acosta (Buenos Aires) intelligence gain, as well, in mental defectives under nialamide treatment.

3. *Psychosomatic and Somatopsychic Illness.* A variety of workers claimed a beneficial effect for nialamide for pain in angina pectoris, cancer, arthritis and in relation to surgery.

4. *Specialty Studies.* McNear (Minnesota) claimed that nialamide administration before the onset of labour reduces the need for sedation and lessens postpartum depression. It also exerts an anti-depressant effect in pre-menstrual depression and teen-age amenorrhoea.

Naranjo (Ecuador) found Niamid a helpful adjuvant in allergic disease and other workers had a similar experience in the dermatoses and anorexia nervosa.

B. PHARMACOLOGY

A number of excellent contributions were made from various countries, the most general and comprehensive of which was probably that of J. A. Schneider *et al.*[3]

The evidence of these contributions sustained the point of view that in the new group of hydrazid derivatives we are dealing with a dual mechanism: (*a*) manifestations due to pharmacological properties of the product itself; and (*b*) the potent inhibition of mono-amine oxidase which causes an increase in the hormone substances adrenaline, noradrenaline, dopamine and serotonin, mainly in the brain, liver and heart.

The ideal drug as a psychic energizer would accordingly be a hydrazid derivative which has a selective action on the brain; and that would mean a good blood-brain barrier diffusion minimizing the effects on the liver, heart, gastro-intestinal tract and circulatory system. Niamid, from clinical trials and pharmacological experiment, answers to this description. An example of a claim for the action of nialamide not referable to MAO inhibition but due to its own pharmacological properties is that of H. Thaler of Vienna, who attributed the favourable response in angina pectoris cases to its blocking effect on the sympathetic nervous system.

III. A BRIEF NOTE ON RESEARCH IMPLICATIONS

The work on Niamid links up in a most stimulating fashion with fundamental considerations in psychiatric genetics which, in its demonstration of specific genetic mechanisms underlying schizophrenia and manic depressive psychosis, already indicates the existence of enzyme blocks. That Niamid, acting at the enzyme level, should selectively affect one of these conditions and not the other, is intriguing and moreover indicates the convergence of fundamental aetiology and therapeutics in this sphere.

Another lead for research is the antagonistic action on the EEG of the 2 groups of drugs we have been considering, viz. the tranquillizers and the mono-amine oxidase inhibitors, with the probability of the brainstem reticular system as the site of action. In the EEG we have a powerful tool for further elucidating this relationship and other neurophysiological aspects.

IV. SUMMARY AND CONCLUSIONS

In the tranquillizers we have a readily administered form of medication, often applicable to the ambulatory patient, for a wide range of psychotic and psychoneurotic conditions. Their impact has already been such as to modify the whole complexion of modern psychiatry.

In the mono-amine oxidase inhibitors, notably Niamid, we have a well tried weapon against endogenous depressions, singularly free from side effects and of long term applicability, with all that implies for a hitherto recurrent illness. The interval before clinical response means its supplementation in the early stages by ECT, in certain cases, notably where suicide is in question. Other fields of application are in the field of mental deficiency, and of pain in relation to medical, surgical, obstetrical and gynaecological conditions.

A link with fundamental aspects of psychiatric genetics and electroencephalographic findings are opening up new prospects for research.

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NOTES AND NEWS : BERIGTE

COMMISSION OF ENQUIRY INTO IONIZING RADIATION

INSPECTIONS

One of the duties of the above Commission is to inspect X-ray installations, not only at hospitals or those used by private medical practitioners (whether specialists or in general practice, dentists or chiropractors), but also non-medical installations such as for industrial, research and for veterinary purposes.

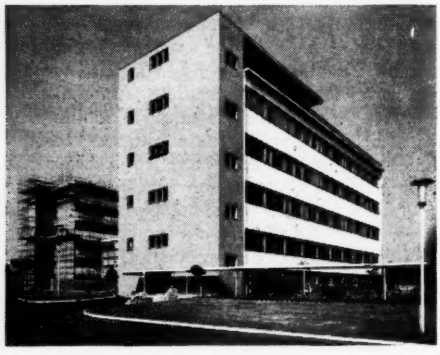
To facilitate the planning of these inspections the Commission requests all owners of equipment producing X-rays to submit details of such equipment to the Secretary, Commission of Enquiry into Ionising Radiation, Room 411, Merino Buildings, Pretorius Street, Pretoria.

* * *

M & B RESEARCH INSTITUTE

Constructional work on a new Research Institute at Dagenham, Essex is now nearing completion and May & Baker Ltd. expect these buildings to be equipped and fully operational by early autumn of this year.

The M & B Research Institute will comprise 3 main buildings: a chemical wing; a central building housing the library, lecture theatre and administrative offices, and a biological wing with ancillary buildings. The entire block will provide over 100,000 sq. ft. of floor space at a cost of over one million pounds.



M & B Research Institute. The Biological Wing has been completed. The Chemical Wing is nearing completion.

The new Research Institute will enable existing research units from various laboratories in the Dagenham Works to be brought together in one coherent group. At the same time it will provide additional facilities for M & B scientists working on expanded research programmes. Close liaison with the present Agricultural and Veterinary Research Station at Ongar, some 12 miles from the main Dagenham Works, will be continued and further development of this Field Research Station will take place.

SIXTH INTERNATIONAL CONGRESS OF INTERNAL MEDICINE

The Sixth International Congress of Internal Medicine, 24–27 August 1960, Basle (Switzerland); organized by the International Society of Internal Medicine (*President*: Sir Russell Brain, F.A.C.P. Hon., London).

President of the Congress: Prof. Dr. A. Gigon, Basle.

Secretary: Prof. Dr. H. Ludwig, Basle.

Principal Subjects of the Congress: Pathogenesy and Therapy in the Edema—Enzymic Regulations in the Clinic.

Panels: Interstitial Nephritis—Nephrosis—Diuretics—Diagnostic Value of the Enzymes—Therapeutic Indications of the Enzymes—Serology in Rheumatic Diseases—Instruction in Internal Medicine.

Lectures on subjects of free choice.

Seventy leading internists from all over the world will take part in the main scientific programme by reading their papers or joining in the panel discussions.

Official Languages: German, French, English. Simultaneous translation for the principal lectures.

Programmes and registration forms for the congress may be obtained from the Secretary of the 6th International Congress of Internal Medicine, Steinentorstrasse 13, Basle 10 (Switzerland). Registrations should reach the Secretary if possible by 30 April 1960.

* * *

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF MEDICINE

MEDICAL GRADUATES ASSOCIATION

Following on the phenomenal success of our first intensive *Post-Graduate Refresher Course for General Practitioners* we are pleased to announce that the *2nd Course* will be held from *Monday to Saturday* 18 *to* 23 *July* 1960.

This course will consist of practical demonstrations, ward rounds and symposia. Senior members of the Hospital and University Departments will participate. The course will include *Paediatrics, Anaesthetics, Dermatology* and *Orthopaedics* in addition to *General Medicine, Surgery, Obstetrics* and *Gynaecology.*

The fee for the course is £5 payable in advance with the application.

Accommodation can be arranged for those desiring it at a nominal fee. Only a limited number of practitioners can be accommodated.

The arrangement whereby one group of 10 doctors, who particularly wanted to see the wealth of clinical material in non-European hospitals and whose practices bring them into contact with Bantu medicine, have their morning ward rounds from 9–11.30 at Coronation Hospital, is being repeated. It must be stressed, however, that the rest of the course, the symposia, demonstrations and lectures are together with the other groups at the Medical School and General Hospital.

Applications should be made to the Medical Graduates Association, Medical School, Hospital Street, Johannesburg, *not later than* 16 *April* 1960.

WEEK-END COURSE IN PSYCHIATRY FOR GENERAL PRACTITIONERS

It has been decided to invite general practitioners to attend a week-end course in *Psychiatry for the General Practitioner,* at Tara Hospital from 20 to 22 May 1960. The Course is planned to be of interest to the general practitioner, and is being held in collaboration with the Medical Graduates' Association of the University of the Witwatersrand.

PROGRAMME

Friday, 20 *May* 1960:

6.00 p.m. *Reception and Sherry.*
7.00 p.m. *Dinner.*
8.00 p.m. *Opening Addresses*:

Prof. L. A. Hurst: *Psychiatry in General Practice.*
Dr. H. Moross: *The Place of Psychiatry in Health Services.*

Saturday, 21 *May* 1960:

9.00 a.m. *Physical Methods of Treatment*: Dr. M. Feldman.
10.15 a.m. *Tea.*
10.30 a.m. *Psychiatric Emergencies in General Practice*: Dr. A. Sidley.
12 midday. *Case Presentation*: Dr. D. Perk; Dr. M. Feldman; Dr. B. W. Levinson; Dr. B. Braude.
1.00 p.m. *Lunch.*
2.00 p.m. *Psychiatric Treatment.*
(*a*) *Psychopharmacotherapy*: Prof. L. A. Hurst.
(*b*) *Presentation on Psychotherapy*: Dr. M. Klass; Dr. L. S. Gillis.
3.30 p.m. *Tea.*
4.00-
5.30 p.m. *Anxiey in Children*: Dr. F. Reinhold.

Sunday, 22 *May* 1960:

9.00 a.m. *Common Psychosomatic Conditions*: Prof. G. A. Elliott.
10.15 a.m. *Tea.*
10.30 a.m. *Psychological Problems in Marriage*: Dr. F. Frankel.
12 midday. Film on *Alcoholism* followed by *Discussion*: Dr. H. E. van Hoepen; Dr. M. C. Frame.
1.00 p.m. *Lunch.*
2.00 p.m. *Psychiatric Problems in the Aged*: Dr. D. Perk.

H. MOROSS,
Superintendent.

PREPARATIONS AND APPLIANCES

OPHTHOCORT

A PARKE-DAVIS NEW OPHTHALMIC PREPARATION

Parke, Davis Laboratories (Pty.) Ltd., have introduced an eye ointment which provides strong, broad-spectrum antibacterial action together with anti-inflammatory activity, for the topical treatment of ocular inflammation.

Description: *Ophthocort* contains 1% chloromycetin (chloramphenicol, Parke, Davis), 0.5% hydrocortisone acetate and 5,000 units of polymyxin B per gm. in a special petrolatum base. *Ophthocort* acts by controlling inflammation whether caused by irritation, trauma, infection, or specific allergens, and thus wards off the danger of excessive vascularization and scarring.

Indications: Because of its proven usefulness against a wide range of pathogens and effective penetration following topical application, *Chloromycetin* has been used extensively against ocular infections. Although the principal pathogenic flora of the eye is staphylococcal, gram-negative organisms are being found in increasing numbers[1] and polymyxin B is particularly active against these new invaders.

It has been statistically derived by Waisbren and Strelitzer[2] that *Chloromycetin* and polymyxin B, the combination provided in *Ophthocort,* is potentially one of the most effective preparations for suppressing cultures of mixed bacteria including staphylococci, Proteus, *Pseudomonas aeruginosa* and other Pseudomonas species, *E. coli,* and *A. aerogenes.*

The use of steroid therapy for inflammatory processes involving the eye has been widely discussed, and it is generally agreed that such treatment is of conspicuous value in restoring the normal appearance of the eye and adding to the comfort of the patient. The inclusion of hydrocortisone acetate in *Ophthocort* provides the appropriate degree of steroid therapy in ocular inflammations.

It is important if a good therapeutic result is to be obtained in ocular diseases to hit the invading organisms hard as well as promptly. In the use of *Ophthocort* the problem of emergence of resistant strains is radically reduced by the prompt hard-hitting antibiotic action of *Chloromycetin* and polymyxin B.

Dosage and Administration: For viral inflammation and non-viral iridocyclitis, with or without ulcer, involving the eye and adnexa, treatment should be directed toward eradicating the etiologic agent and controlling the inflammatory response of these highly sensitive tissues. Although marked variation is seen both in patients and pathogens, the physician may consider the following suggested dosage schedule in outlining a course of therapy.

Suggested Dosage Schedule: First 24 to 48 hours: *Ophthocort* should be applied to the affected eye 2–4 times daily. Thereafter, continue until the eye has appeared normal for 48 hours.

Physicians are reminded that treatment with *Ophthocort* should not be stopped abruptly, since relapse is more likely to occur on sudden cessation of therapy than when therapy is tapered slowly to conclusion. Should relapse occur, the schedule of treatment already outlined should be resumed.

When hydrocortisone is applied locally in treating bacterial diseases of the eye, care must be exercised to make sure the condition is not actually progressing while the external appearance improves. The antibacterial action of *Chloromycetin* and polymyxin B reduces this probability to a minimum; neverthe-

less, as every physician knows, there is no substitute for careful observation of the patient.

Package Information: *Ophthocort* Ophthalmic Ointment is supplied in 1/8 oz. tubes containing 1% *Chloromycetin* (Chloramphenicol, Parke, Davis), 0.5% hydrocortisone acetate, and 5,000 units of polymyxin B sulphate per gm.

REFERENCES

1. Smith, C. H.: The E.E.N.T. Monthly **34**: 580, 1955.
2. Waisbren, B. A. and Strelitzer, C. L.: Antibiotics Annual, 1956-57; also Arch. Int. Med. **99**: 744, 1957.

REVIEWS OF BOOKS

ARTERIAL EMBOLISM

Arterial Embolism in the Limbs: *The Clinical Problem and its Anatomical Basis*. By A. L. Jacobs, M.A., D.M. (Oxon.), F.R.C.P. (1959. Pp. 197 + Index. With 37 figs. 35s. Postage 1s. 10d.). Edinburgh and London: E. & S. Livingstone Ltd.

This is a comprehensive and systematic study of this problem. The historical section covers the subject broadly, starting with Harvey's publication in 1628 and describing the first successful embolectomy, the origin of the theory of embolic-arteriospasm and the history of anticoagulant therapy.

The incidence of limb embolism in mitral stenosis is discussed with the conclusion that this is a relatively frequent occurrence and that transient acute ischaemic symptoms often occur with full recovery. The aetiology of arterial embolism is considered statistically in relation to the anatomical sites of embolism and there is also discussion of thrombosis following embolism.

Silent embolism is a clinical feature and a very thorough discussion is given of the clinical examination in these cases. The differential diagnosis with the outcome and the prognosis in these cases is dealt with. Discussion also covers anatomical variations in arterial collaterals and the question of arterial spasm is considered in detail.

The clinical evolution of the ischaemic symptoms and the extent of the ischaemic signs in limb embolism and embolic migration are enlarged upon.

This is a book which undoubtedly is a valuable contribution to vascular surgery. Any surgeon dealing with arterial lesions and vascular surgery should include this book in his library. It is a practical book and the *Summary of Main Conclusions* gives each conclusion and the reference chapter where the subject is dealt with more comprehensively. There is an extensive bibliography and, in all, a well presented and thorough exposition of the subject.

PSYCHIATRIC SERVICES AND ARCHITECTURE

Psychiatric Services and Architecture. A. Baker, R. Llewelyn Davies and P. Sivadon. World Health Organization: Public Health Papers, 1959, No. 1; 50 pages. 2s. 6d. Pretoria: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724.

It has been said that the perfect mental hospital does not exist, and could hardly be expected to evolve until its functions were analysed and it was matched to them in design. We are, as is evident from the frequency of experiments with mental patients, in the midst of just such an analysis of the functions of these hospitals; this is part and parcel of the revolutionary re-assessment now taking place in psychiatry of the bases and assumptions upon which the treatment of mental patients is founded.

This booklet attempts an analysis, not only of the planning and management of psychiatric hospitals, but also of the structure and function of other psychiatric services such as out-patient departments, psychiatric wards in general hospitals, rehabilitation facilities, and other mental health services. It is the joint work of two psychiatrists and an architect who has specialized in hospital architecture, but it also takes account of the comments and suggestions of 29 psychiatrists and 4 architects from various countries who read the original manuscript. It thus represents an international approach to the problem of how psychiatric services can best be organized in the interests of the patients and be given suitable architectural expression. The types of buildings proposed are worlds apart from the gloomy, prison-like mansions which until recently were regarded in many parts of the world as the only appropriate places in which to incarcerate mental patients; the approach to the patient is based upon the desire to reintegrate him into society with all possible dispatch, and to provide him with surroundings that will contribute to that end.

CORRESPONDENCE

THE PHYSICIAN'S PRAYER

To the Editor: The indignant character of my letter concerning Dr. A. Rieck's adaptation of *The Physician's Prayer* was simply because it appeared that he was taking credit for somebody else's work. Dr. Rieck's explanations have clarified the matter and, of course, I hasten to apologize for expressing such thoughts on plagiarism; clearly this is not so.

S. Levin,
M.B., M.R.C.P.E., D.C.H.

67, Jenner Chambers,
Johannesburg.

TUBERCULIN JELLY

To the Editor: I refer to the letter in your Correspondence Columns in the issue of 12 March 1960, p. 120.

Tuberculin Jelly (Perkutan-Tuberkulin Salbe) is made by Farbwerke Hoechst A.G., Frankfurt a.M. (Germany) and distributed by Dr. E. Fresenius, Bad Homburg v.d.H. (Germany), who also supplies a special adhesive tape for the patch test.

I had no difficulty in obtaining both through our local chemist.

V. M. Victor.

P.O. Box 337,
Swakopmund, South West Africa.